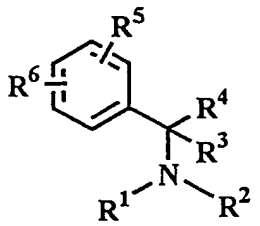
CLAIMS

1. A compounds of formula (I)



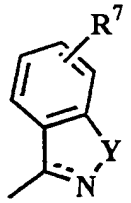
(I)

wherein R^1 and R^2, which may be the same or different, are each selected from C_{6-12}aryl, C_{2-14}heteroaryl, C_{6-12}arylC_{1-6}alkyl, C_{2-14}heteroarylC_{1-6}alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C_{1-6}alkoxy, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{4-6}cycloalkenyl, C_{6-12}aryl, C_{2-14}heteroaryl, halogen, amino, hydroxy, haloC_{1-6}alkyl, nitro, C_{1-6}alkylthio, sulphonamide, C_{1-6}alkylsulphonyl, hydroxy-C_{1-6}alkyl, C_{1-6}alkoxycarbonyl, carboxyl, carboxyC_{1-6}alkyl, carboxamide and C_{1-6}alkylcarboxamide), hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{4-6}cycloalkenyl, C_{2-6}alkenyl, C_{2-6}alkynyl and C_{1-6}alkoxyC_{1-6}alkyl (where the alkyl, cycloalkyl, cycloalkenyl, alkenyl, alkynyl, or alkoxyalkyl moieties may be optionally substituted by one or more substituents selected from amino, halogen,hydroxy, C_{1-6}alkylcarboxamide, carboxamide, carboxy, C_{1-6}alkoxycarbonyl, C_{1-6}alkylcarboxy and carboxyC_{1-6}alkyl) or one of R^1 and R^2 are as hereinbefore defined and one is hydroxy;

R^3 and R^4, which may be the same or different, are each selected from C_{6-12}aryl, C_{2-14}heteroaryl, C_{6-12}arylC_{1-6}alkyl, C_{2-14}heteroarylC_{1-6}alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C_{1-6}alkoxy, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{4-6}cycloalkenyl, C_{6-12}aryl, C_{2-14}heteroaryl, halogen, amino, hydroxy, haloC_{1-6}alkyl, nitro, C_{1-6}alkylthio, sulphonamide, C_{1-6}alkylsulphonyl, hydroxyC_{1-6}alkyl, C_{1-6}alkoxycarbonyl, carboxyl, carboxyC_{1-6}alkyl, C_{1-6}alkylcarboxamide and carboxamide), hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkylC_{1-6}alkyl, C_{4-6}cycloalkenyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy-C_{1-6}alkyl, halo C_{1-6}alkyl, haloC_{2-6}alkenyl, haloC_{2-6}alkynyl, cyano, carboxyl, C_{1-6}alkylcarboxy and carboxyC_{1-6}alkyl (where the alkyl, cycloalkyl, cycloalkenyl, alkenyl, alkynyl, or alkoxyalkyl moieties may be optionally

substituted by one or more substituents selected from amino, hydroxy, C_{1-6}alkylcarboxamide, carboxamide, carboxy, C_{1-6}alkoxycarbonyl, C_{1-6}alkylcarboxy and carboxyC_{1-6}alkyl); or one of R^3 or R^4 together with one of R^1 or R^2 and the N atom to which it is attached form a 5- or 6-membered heterocyclic ring.

R^5 represents one or more ring substituents selected from halogen, hydrogen C_{1-6}alkyl and C_{1-6}alkoxy; and
R^6 represents a single ring substituent of formula:



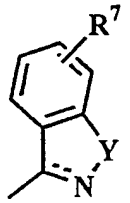
wherein the dotted line represents an optional bond; Y is oxygen or -NR^8
(where R^8 is hydrogen or C_{1-6}alkyl) and R^7 represents one or more substituents selected from hydrogen, halogen, haloC_{1-6}alkyl, C_{1-6}alkyl and C_{1-6}alkoxy; or
a pharmaceutically acceptable salt or solvate thereof.

2. A compound according to claim 1 wherein R^1 and R^2, which may be the same or different, are each independently selected from C_{6-12}aryl, C_{2-14}heteroaryl, C_{6-12}arylC_{1-6}alkyl, C_{2-14}heteroarylC_{1-6}alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C_{1-6}alkoxy, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{4-6}cycloalkenyl, C_{6-12}aryl, C_{2-14}heteroaryl, halogen, amino, hydroxy, haloC_{1-6}alkyl, nitro, C_{1-6}alkylthio, sulphonamide, C_{1-6}alkylsulphonyl, hydroxyC_{1-6}alkyl, carboxyl, carboxy-C_{1-6}alky, carboxamide and C_{1-6}alkylcarboxamide), hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{4-6}cycloalkenyl, C_{2-6}alkenyl, C_{2-6}alkynyl and C_{1-6}alkoxyC_{1-6}alkyl (where the alkyl, cycloalkyl, cycloalkenyl, alkynyl, or alkoxyalkyl moieties may be optionally substituted by one or more substituents selected from amino, hydroxy, C_{1-6}alkylcarboxamide, carboxamide, carboxy and carboxyC_{1-6}alkyl) or one of R^1 and R^2 are as hereinbefore defined and one is hydroxy;
R^3 and R^4, which may be the same or different, are each independently selected from C_{6-12}aryl, C_{2-14}heteroaryl, C_{6-12}arylC_{1-6}alkyl,

C_{2-14}heteroaryl-C_{1-6}alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C_{1-6}alkoxy, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{4-6}cycloalkenyl, C_{6-12}aryl, C_{214}heteroaryl, halogen, amino, hydroxy, haloC_{1-6}alkyl, nitro, C_{1-6}alkylthio, sulphonamide, C_{1-6}alkylsulphonyl, carboxamide and C_{1-6}alkylcarboxamide), hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{4-6}cycloalkenyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxyC_{1-6}alkyl, cyano, carboxyl and carboxyC_{1-6}alkyl;

R^5 represents one or more ring substituents selected from halogen, hydrogen, C_{1-6}alkyl and C_{1-6}alkoxy; and

R^6 represents a single ring substituent of formula:



wherein the dotted line represents an optional bond; Y is oxygen or -NR^8 (where R^8 is hydrogen or C_{1-6}alkyl) and R^7 is hydrogen, halogen, C_{1-6}alkyl or C_{1-6}alkoxy;or a pharmaceutically acceptable salt or solvate thereof.

3. A compound according to claim 1 or 2 wherein one of R^1 and R^2 is hydrogen and the other is C_{6-12}arylC_{1-6}alkyl (where the alkyl or aryl moiety may be optionally substituted by one or more ring substituents selected from C_{1-6}alkoxy and C_{2-14}heteroaryl); R^3,R^4 and R^5 are hydrogen, Y is oxygen, the dotted line represents a bond and R^7 is hydrogen or halogen; or a pharmaceutically acceptable salt or solvate thereof.

4. A compound of formula (I) according to any of claims 1 to 3 wherein R^1 and R^2 are both hydrogen; one of R^3 and R^4 is hydrogen and the other is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxyC_{1-6}alkyl or C_{6-12}arylalkyl; R^5 is hydrogen, Y is oxygen or -NCH_3, the dotted line represents a bond and R^7 is hydrogen or halogen; or a pharmaceutically acceptable salt or solvate thereof.

5 A compound according to claim 1 selected from:
2-(1,2-Benzisoxazol-3-yl)-benzenemethanamine;
2-(1,2-Benzisoxazol-3-yl)-α-2-propenyl-benzenemethanamine;
(R)-(+)-2-(1,2-Benzisoxazol-3-yl)-α-2-propenyl-benzenemethanamine;
(S)-(–)-2-(1,2-Benzisoxazol-3-yl)-α-2-propenyl-benzenemethanamine;
2-(1,2-Benzisoxazol-3-yl)-α-butyl-benzenemethanamine;
2-(1,2-Benzisoxazol-3-yl)-α-2-propynyl-benzenemethanamine;
2-(1-Methyl-1*H*-indazol-3-yl)-α-2-propenyl-benzenemethanamine;
(-)-2-(6-chloro-1,2-benzisoxazol-3-yl)-a-2-propynyl-benzenemethanamine;
(S)-(-)-2-(6-chloro-1,2-benzisoxazol-3-yl)-a-2-propenyl-benzene-methanamine;
and pharmaceutically acceptable salts and solvates thereof.

6. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to any of claims 1 to 54 for use in therapy.

7. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to any of claims 1 to 5, in the manufacture of a medicament for the treatment or prevention of depression.

8. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to any of claims 1 to 5, in the manufacture of a medicament for the treatment or prevention of conditions selected from:

- anxiety disorders, including phobic neuroses, panic neuroses, anxiety neuroses, post-traumatic stress disorder and acute stress disorder;
- attention deficit disorders;
- eating disorders, including obesity, anorexia nervosa and bulimia;
- personality disorders, including borderline personality disorders;
- schizophrenia and other psychotic disorders, including schizo affective disorders, dilusional disorders, shared psychotic disorder, brief psychotic disorder and psychotic disorder;
- narcolepsy-cataplexy syndrome;
- substance related disorders;
- sexual function disorders; and
- sleep disorders.

9. A pharmaceutical formulation comprising a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to claim 1, together with a pharmaceutically acceptable carrier thereof.

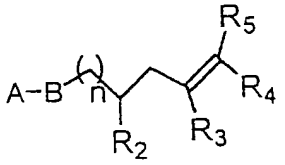
10. A method for the treatment or prevention of a psychiatric disorder in an animal, which comprises administering to said animal an effective amount of an I_h channel modulator.

11. A method according to claim 10, wherein the psychiatric disorder is depression, anxiety or psychosis.

12. A method according to claim 10, wherein the I_h channel modulator blocks conductance of the I_h channel and/or the open probability.

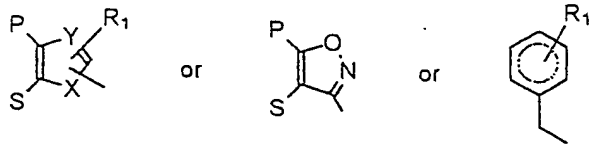
13. A method according to claim 12, wherein the I_h channel modulator has a plC_{50} of 5 to 12 in an I_h channel modulator functional assay.

14. A compound of formula (I)



(I)

wherein A is a group selected from (a), (b) or (c):



(a) (b) (c)

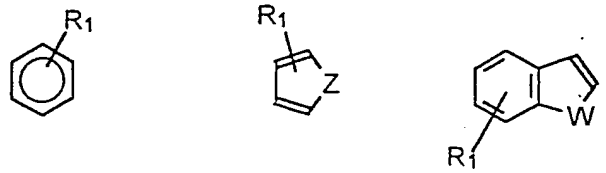
wherein Y is CH or N;

X is O, S, CH=CH, or CH=N;

P and S, which may be the same or different, each represent hydrogen, C_{1-4}alkyl, C_{1-3}alkoxy, cyano, halogen, trifluromethyl, phenyl or pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C_{1-3}alkyl; or P and S together with the ethylene group to which they are bonded form a 1,2-phenylene, a pyridinediyl (including 2,3- and 3,4-pyridinediyl), or a 1-cyclohexen-1,2-diyl group, which groups may be optionally substituted by one or more substituents selected from hydrogen, C_{1-4}alkyl, C_{1-3}alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C_{1-3}alkyl;

R_1 represents one or more ring substituents selected from hydrogen, C_{1-4}alkyl, C_{1-3}alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C_{1-3}alkyl;

B is a bivalent radical derived from an aromatic group selected from (d), (e) or (f):



(d) (e) (f)

wherein

Z is O or S;

W is O, S or CH=CH,

R_1 is as hereinbefore defined;

R_2 is NH_2;

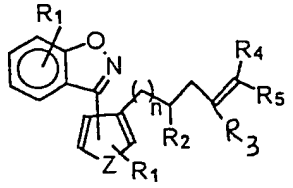
R_3, R_4, and R_5, which may be the same or different, each represent halogen, C_{1-4}alkyl or hydrogen, or R_4 and R_5 together form a carbon-carbon bond;

n is 0 or 1;

or a physiologically acceptable salt or solvate thereof;

with the proviso that when A is group (b) wherein P and S together with the ethylene group to which they are bonded form a 1,2-phenylene group, which group may optionally be substituted by one or more substituents selected from hydrogen, C_{1-4}alkyl, C_{1-3}alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C_{1-3}alkyl; R_2, R_3, R_4 and R_5 are as herein before defined and n is 0; then B is a group (e) or (f).

15. A compound according to claim 14 of formula (IA)

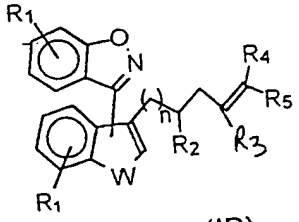


(IA)

wherein Z, R_1, R_2, R_3, R_4 and R_5 are as defined in claim 14 and n is 0;

or a physiologically acceptable salt or solvate thereof.

16. A compound according to claim 14 of formula (IB)

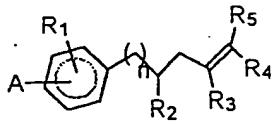


(IB)

wherein W, R_1, R_2, R_3, R_4 and R_5 are as defined in claim 14 and n is 0;

or a physiologically acceptable salt or solvate thereof.

17. A compound according to claim 14 of formula (IC)



(IC)

wherein A, R_1, R_2, R_3, R_4 and R_5 are as defined in claim 1 and n is 0 or 1, preferably n is 0; or a physiologically acceptable salt of solvate thereof; with the proviso that A is not a group (b) wherein P and S together with the ethylene group to which they are bonded form a 1,2-phenylene group, which group may be optionally substituted by one or more substituents selected from hydrogen, C_{1-4}alkyl, C_{1-3}alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C_{1-3}alkyl; R_2, R_3, R_4 and R_5 are as defined in claim 1 and n is 0;

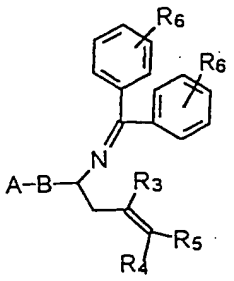
or a physiologically acceptable salt or solvate thereof.

18. A pharmaceutical formulation containing a compound of formula (I) or a physiologically acceptable salt or solvate thereof, as defined according to claim 14, together with a pharmaceutically acceptable carrier therefor.

19. A method for the treatment or prevention of a psychiatric disorder in an animal, which comprises administering to said animal an effective amount of a compound of formula (I) or a physiologically acceptable salt or solvate thereof, as defined according to claim 14.

20. A process for preparing a compound of formula (I) as defined in claim 14 or a physiologically acceptable salt or solvate thereof; which comprises:

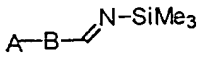
(A) reacting a compound of formula (II)



(II)

wherein A, B, R_3, R_4 and R_5 are as defined in claim 1 and R_6 is hydrogen or halogen, with a hydrolysing agent;

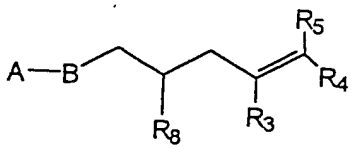
(B) reacting an imine of formula (IIA)



(IIA)

wherein A and B are as defined in claim 10, with an appropriate organometallic reagent in the presence of an inert solvent; or

(C) for compounds of formula (I) wherein n is 1, the reduction of a compound of formula (XV)



(XV)

wherein A, B, R_3, R_4 and R_5 are as defined in claim 1 and R_8 is an azido group, and

where necessary or desired, following processes A to C above, any one or more of the following further steps in any order may be performed:

(i) removing any remaining protecting group(s);

(ii) converting a compound of formula (I) or a protected form thereof into a further compound of formula (I) or a protected form thereof;

(iii) converting a compound of formula (I) or a protected form thereof into a pharmaceutically acceptable salt or solvate of a compound of formula (I) or a protected form thereof;

(iv) converting a pharmaceutically acceptable salt or solvate of a compound of formula (I) or a protected form thereof into a compound of formula (I) or a protected form thereof;

(v) converting a pharmaceutically acceptable salt or solvate of a compound of formula (I) or a protected form thereof into another pharmaceutically acceptable salt or solvate of formula (I);

(vi) where the compound of formula (I) is obtained as a mixture of (R) and (S) enantiomers resolving the mixture to obtain the desired enantiomer;

(vii) cleavage of a compound of formula (I) from a solid phase resin.

21. A method for identifying compounds useful for the treatment or prevention of psychiatric disorders by measuring the level of I_h channel modulation in an I_h channel modulation assay.

22. A method for identifying compounds useful for the treatment or prevention of psychiatric disorders by measuring the level of I_h channel modulation in an I_h channel modulation assay comprising:

- taking a brain slice, or a cultured brain slice, or ganglia of the peripheral nervous system, or primary

cell cultures of central and/or peripheral nervous tissue, or cell lines expressing I_h channels

- incubating and/or exposing these cells and tissues to test compounds and
- measuring whether these test compounds affect conductance of the I_h channel and/or the open probability.